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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/826,509	04/05/2001	Karin Lehmann-Bruinsma	AREN-0207	7872

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EXAMINER

LI, RUIXIANG

ART UNIT

PAPER NUMBER

1646

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Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	09/826,509	LEHMANN-BRUIINSMA ET AL.	
	<b>Examiner</b> Ruixiang Li	<b>Art Unit</b> 1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) Responsive to communication(s) filed on 28 February 2002.
- 2a) This action is FINAL.                    2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) Claim(s) 101-177 is/are pending in the application.
- 4a) Of the above claim(s) 106-177 is/are withdrawn from consideration.
- 5) Claim(s) \_\_\_\_\_ is/are allowed.
- 6) Claim(s) 101-105 is/are rejected..
- 7) Claim(s) \_\_\_\_\_ is/are objected to.
- 8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on April 5, 2001 is/are: a) accepted or b) objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) The proposed drawing correction filed on \_\_\_\_\_ is: a) approved b) disapproved by the Examiner.  
If approved, corrected drawings are required in reply to this Office action.
- 12) The oath or declaration is objected to by the Examiner.

#### Priority under 35 U.S.C. §§ 119 and 120

- 13) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) All b) Some \* c) None of:  
 1. Certified copies of the priority documents have been received.  
 2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).  
a) The translation of the foreign language provisional application has been received.
- 15) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

#### Attachment(s)

- |  |  |
|--|--|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)                                  | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ . |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                         | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)  |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) <u>3</u> . | 6) <input type="checkbox"/> Other: _____                                     |

## **DETAILED ACTION**

### ***Election/Restrictions***

1. Applicants' election with traverse of Claims 1, 14, 101, and 102, drawn to SEQ ID NO: 449, in Paper No. 5 is acknowledged. The traversal is on the ground that the current application is directed to a method that is applicable to individual receptors whereas the receptors themselves are not claimed. This is not found persuasive because examination of a method does require examining a receptor that is applied to the method and examination of more than one receptor (one amino acid/nucleotide sequence) requires non-cohesive searches and considerations, which constitute an undue search burden on the office, given the ever-increasing size of the database.

The requirement is still deemed proper and is therefore made FINAL.

2. Applicants' claim amendment of in Paper No. 5 is acknowledged. Claims 1-100 have been canceled, Claim 101 has been amended, and new claims 103-177 have been entered. Claims 101-105 are pending and under consideration.

### ***Priority***

3. Acknowledgment is made of a claim for domestic priority under 35 U.S.C. 119(e) to a provisional application, 60/195,747, filed on 04/07/2000.

***Objections to the Disclosure***

4. The disclosure is objected to because of the use of the trademarks in this application, for example, Flash plates<sup>TM</sup> and Wallac<sup>TM</sup> scintistrips (page 71, line 14) and Scinti<sup>®</sup> strips (page 72, line 1). They should be capitalized wherever they appear and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

***Claim Rejections—35 USC § 112, 2<sup>nd</sup> paragraph***

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claim 103 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 103 is indefinite because it is unclear what "the parallel agonists" mean (the term is not defined in the specification). There is also a likely typographical error in the claim, part (d), line 3; it appears that "is" should be "as". In addition, the procedures set forth by the claim do not necessarily achieve the goal of identifying a compound having an activity selected from the group consisting of inverse agonist,

parallel agonist, and partial agonists, as defined by the claim preamble. Additional steps need to be added.

***Claim Rejections—35 USC § 102***

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C. 122(b). Therefore, this application is examined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

8. Claims 101-104 are rejected under 35 U.S.C. 102(b) as anticipated by Herrick-Davis et al. (Annals of the New York Academy of Sciences 861:140-145, 1998).

Herrick-Davis et al. teach that 5-HT<sub>2c</sub> serotonin receptor, a G-protein coupled receptor, can be rendered constitutively active by changing amino acid 312 (<sup>or</sup> 3<sup>rd</sup> intracellular loop) from serine to lysine (S312K) (See, for example, *Abstract*). Herrick-Davis et al. also teach a method of using constitutively active 5-HT<sub>2c</sub> serotonin receptor mutants for identifying agonists, antagonists, and inverse agonists (pages 141-142; Fig. 1). Herrick-Davis et al. further teach a radioligand binding assay for assessing the impact of such agonists, antagonists, or inverse agonist on the binding

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of natural ligand to both natural 5-HT2c serotonin receptor and its constitutively active mutants (pages 141 and 143; Table 1). Some of the inverse agonists identified apparently do not have high binding affinity for the 5-HT2c serotonin receptor (allosteric modulators; Table 1). Thus, Herrick-Davis et al. meets the limitations of claims 101-104.

9. Claims 101-104 are rejected under 35 U.S.C. 102(e) as anticipated by Behan et al. (U.S. Patent No. 6,150,393, November 21, 2000, filed on October 15, 1999).

Behan et al. teach non-endogenous, constitutively activated forms of the human 5-HT2a and human 5-HT2c serotonin receptors (G-protein coupled receptors) and uses of such receptors to screen candidate compounds and to identify agonists, partial agonists, antagonists, and inverse agonists. U.S. Patent No. 6,150,393 by Behan et al. has nearly identical specification as the instant application, except the subject matter of the instant application is related to non-endogenous, constitutively activated forms of human 5-HT6 serotonin receptor. U.S. Patent No. 6,150,393 meets all the limitations of the claims 101-104 (See, in particular, columns 2, 5, 6, 13-18).

***Claim Rejections—35 USC § 103 (a)***

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

11. Claim 105 is rejected under 35 U.S.C. 103(a) as being unpatentable over Herrick-Davis et al. or Behan et al. in view of Kohen et al. (*IDS*, AY; *J. Neurochem.* 66:47-56, 1996).

Both Herrick-Davis et al. and Behan et al. teach a method for identifying agonists, antagonists, partial agonists, inverse agonists using non-endogenous, constitutively activated forms of human 5-HT<sub>2a</sub>/5-HT<sub>2c</sub> serotonin receptors, as applied to claims 101-104. Both Herrick-Davis et al. and Behan et al. fail to teach the use of non-endogenous, constitutively activated forms of human 5-HT<sub>6</sub> serotonin receptors.

Kohen et al. teach the nucleotide and amino acid sequences of a human 5-HT<sub>6</sub> serotonin receptor. The amino acid sequence taught by Kohen et al. has only a single amino acid difference with SEQ ID NO: 449.

Therefore, it would have been obvious for one skilled in the art to make the non-endogenous, constitutively activated forms of human 5-HT<sub>6</sub> serotonin receptor from the cDNA sequence taught by Kohen et al. using the approach taught by either Herrick-Davis et al. or Behan et al. and to include such mutants in the method of Herrick-Davis et al. or Behan et al. One would have been motivated to do so because serotonin receptors are an important class of G-protein coupled receptors and are implicated in important biological functions as taught by Behan et al. (Icolumn 1 last paragraph).

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ruixiang Li whose telephone number is (703) 306-0282. The examiner can normally be reached on Monday-Friday, 8:30 am-5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, can be reached on (703) 308-6564. The fax phone number for this Group is (703) 305-3014 or (703) 308-4242.

Communications via Internet e-mail regarding this application, other than those under 35 U.S.C. 132 or which otherwise require a signature, may be used by the applicant and should be addressed to [yvonne.eyler@uspto.gov].

All Internet e-mail communications will be made of record in the application file. PTO employees do not engage in Internet communications where there exists a possibility that sensitive information could be identified or exchanged unless the record includes a properly signed express waiver of the confidentiality requirements of 35 U.S.C. 122. This is more clearly set forth in the Interim Internet Usage Policy published in the Official Gazette of the Patent and Trademark on February 25, 1997 at 1195 OG 89.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Ruixiang Li  
Examiner  
March 20, 2002

*Elizabeth C. Kemmerer*

ELIZABETH KEMMERER  
PRIMARY EXAMINER